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The University of Toronto Medical Journal

VOL. V

JANUARY, 1928

No 3

EDITORIAL.

The holiday season with its festivities and frivolities is over, and we are again assembled in battle array, to meet the problems which will confront us in laboratory and in hospital. There will be many allurements to draw the soldier of science from the firing line in the shape of social diversions, and extra-curricular activities, but the wise student will continually keep uppermost in his mind the objective to be gained—a mastery of the art and science of medicine which will make him an efficient unit of society. The secret of victory in this battle is contained in “the master word of medicine”—work. The objective is to be gained only through days of concentration and observation, and nights of effort. The army in which we fight is efficiently generalised and officered by men who are willing to lead us as far as our efforts enable us to go. They have explored the ground which is before us, and will guide us skilfully around the pitfalls which await us. Under their direction no earnest student need fear that he will become a casualty in the examination skirmish. Forward, then, and may the close of the year bring to all that deep satisfaction which follows the successful accomplishment of that which has cost us real effort, and which will be productive of lasting results.

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The attention of the readers of the “Journal” is called to the leading article of this issue, the address delivered by Dr. Routley, Secretary of the Canadian Association, to the Medical Society, on Dec. 11, 1927. In this article

Dr. Routley outlines the opportunities awaiting the young graduate in this our own country, Canada. There has been an increasing tendency on the part of our graduates of recent years to seek situations across the line in the United States. There is a mistaken impression abroad that the profession is overcrowded in Canada, and that there are much greater opportunities in the United States. When one considers that according to the American Medical Association Journal that there is one practitioner of medicine to every seven hundred and fifty of the population in the United States, whereas, as Dr. Routley points out, there is only one practitioner to every thousand of the population in Canada, it does not seem on the face of it that opportunities are greater on the other side. Only in the Province of Ontario are the numbers of the medical profession in proportion to the population equal to the numbers in the States. In fact there is no country in the world where the medical profession is so overcrowded as in the United States. Our western provinces, the newer portions of Ontario, and the maritime provinces, offer ample opportunities to the graduate who will go where he is needed.

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It may be that students in the Faculty of Medicine in the University of Toronto do not appreciate why the palm has been awarded our school by the Educational Committee of the Carnegie Institute. Nearness does not always lend enchantment to the view. However, when three of our last year's graduates, viz., C. E. Snell-

ing, P. Murray, and Homer Bull, entered into competition with four hundred medical graduates from all over the United States on Part II. of the National Board examination, and all of them made places on the "Honor List," i.e., among the first ten, we feel that we have some reason to feel proud

of our training. When one realizes that only the more ambitious American students take the National Board Examinations, the significance of the high standing taken by Toronto men is all the greater. The Journal takes this opportunity of congratulating these men on their achievement.

***An Address to An Open Meeting of the University of Toronto Medical School.**

By Dr. T. C. Routley,
General Secretary, Canadian Medical Association.

It is always a joy to me, in the course of my work, to meet students in medicine, and, particularly do I appreciate the privilege of meeting this group in my Alma Mater, and under the auspices of the Medical Society of which I once had the honour to be President.

In listening to the remarks of your President, it was with sorrow and regret that I learned that the officers of the Medical Society are now elected very largely by acclamation. That does not suggest a healthy condition in your Society. In days gone by, election day was one of the biggest of the year. All offices were keenly contested. I would express the hope that that day may again return.

I am particularly happy to be associated on your programme to-night with Doctor Primrose, who, in addition to being your Dean, is Chairman of the Council of the Canadian Medical Association, the body of which I have the honour to represent here to-night, and in whose hands rests the destiny of organized medicine throughout the Dominion of Canada. I have not prepared for you a formal address. Rather do I prefer to talk for a little while on "The Practice of Medicine in Canada" and endeavour to clothe the subject

with some remarks and observations which I have gleaned during the nine years in which it has been my pleasure to be associated with organized medicine.

The Great War taught us many which I have gleaned during the nine exclusively than the value of organization. On my return from overseas I was asked if I would accept the position of Secretary of the Ontario Medical Association. Although it was an organization some thirty-seven years old, it had less than 500 members, some ten or twelve branches and a budget of something less than \$1,000 a year. To-day the Ontario Medical Association has more than 2,000 members, some forty-seven branches and a budget exceeding \$20,000 a year. Concomitantly with the development in this Province, the profession in the other provinces also became active, until to-day we have in Canada nine virile provincial Medical Associations banded together in the Canadian Medical Association. This nation-wide organization is inspired and actuated by one great ambition, namely, to assist the medical practitioner to be happy and efficient in his task.

What is it that prompts a man to enter medicine? Let us hope that, in most cases, it is the desire to serve. The Federal Income Tax Department would

*Hart House, Toronto, Dec. 7th, 1927.

reveal the fact that there are few huge incomes made in the practice of medicine. The medical profession demands the very best in brain and body, and does not offer great reward by way of financial returns. A newspaper editor stated that in answer to a questionnaire circulated among the freshmen of a certain medical school, 70 % of the students replied that their primary object in entering medicine was to serve humanity. Very creditable, indeed; but not so commendable was the statement that the majority of these freshmen had already decided what specialty they were going to follow after graduation. I would strongly urge men at the beginning of their medical course to eschew the tendency to choose a specialty, but rather to endeavour to acquire a broad technical knowledge of the whole field of medicine, and, furthermore, to take every opportunity of learning something of the art of medicine. This latter involves an understanding of your fellow-men; training your powers of intuition and judgment so that you will be a serviceable man in the field of your chosen profession. To this end, do not keep your nose too close to the grindstone. Take part in athletics and social functions; meet the other fellow's girl,—not with the object of stealing her—but meet her, anyway. Consequently endeavour to train your brain to have a true appreciation of the situation which will confront you when a patient presents himself and says, "Doctor, I am sick."

When college days are over—what then? If you can possibly afford it, take at least two years internship in a hospital. If you cannot afford to do this, do it anyway. I cannot advise this too strongly and I speak with a knowledge gained from personal contact with upwards of 5,000 medical practitioners in Canada. Where are you going to take this hospital training? During the past few years I have noted that about 40 per cent. of our medical graduates have entered hospitals in the country of our neighbour to the south. I hope that in future the majority of

our graduates will find appointments here at home in Canada. The Canadian Medical Association is planning to be of assistance to the graduate in this regard. In the immediate future, the Association is to have a full-time assistant secretary in charge of a new department of Hospital Service. The hospitals of Canada are to be visited and the Association hopes among other things to be in a position to advise graduates of the opportunities which exist throughout our country for internship positions.

I find that the prospect of post graduate study in England appeals strongly to a large number who have been out in practice for a while, and also to some of our recent graduates. To such I would say, if you contemplate going to England to study, the Canadian Medical Association will be glad to give you a letter of introduction to the Secretary of the British Medical Association, who will place at your disposal the facilities of that great organization to assist you in any possible way.

Immediately following graduation or your hospital internship, comes the important step of securing a license to practice. In more ways than one, this is a vital problem confronting every graduate. There are at present ten licensing bodies in Canada, nine provincial and one Dominion. In my judgment, there are altogether too many examinations. Doctor Primrose, in addition to being Chairman of the Council of the Canadian Medical Association, is also chairman of the Conference on the Medical Services in Canada,—a group which has now held two meetings in Ottawa under the aegis of the Minister of Health for Canada, and which was organized for the purpose of facilitating and improving the practice of medicine in Canada. At our last conference, a resolution was passed suggesting that steps should be taken to bring about a condition whereby students, upon completing their final examination for degree would by this same examination, qualify for a license

to practise in any part of Canada. If a candidate is a fit man to receive a diploma from his university, and as every one of the universities teaching medicine in Canada are of such high standing, then I say there seems to be no reasonable excuse for subjecting the candidate to a second examination unless it could be argued that the second examination requires him to go over his work a second time. When all the pros and cons are carefully weighed, I am strongly of the opinion that it should not be impossible to work out a plan of one examination for degree and license.

Now that degree, license, hospital experience (and maybe wife) have been obtained, the great question is "Where am I to settle?" Just here let me say that it is my sincere hope that most of you will be found somewhere under this old Union Jack which floats over the four-thousand-mile stretch from the Atlantic to the Pacific, which we call Canada. Statisticians tell us that it takes \$20,000 to make a doctor. While a part of this is paid by the student himself, the fact remains that you owe the State a great deal for your education. This, in turn, implies that you have a real obligation to the country which has trained you, and it is well to bear this in mind before leaving for foreign fields as a final place of abode.

As to the distribution of the medical profession in this country, the following table may be of interest:

Province.	Population.	No. of Doctors.
British Columbia ..	568,000	550
Alberta	608,000	540
Saskatchewan	821,000	575
Manitoba	639,000	513
Ontario	3,146,000	3,900
Quebec	2,562,000	2,400
New Brunswick...	407,000	236
Nova Scotia	540,000	460
P. E. Island.....	87,000	59
	9,378,000	9,233

From the foregoing you will observe that in Canada there is approximately one Doctor to every thousand of population. Yearly, one per cent. is removed by death, one per cent. by retirement, and probably one per cent. for other reasons. Thus, from all causes, there is a professional loss of 300 a year. The medical schools of Canada graduate yearly approximately 400 students. It will, therefore, be noted that the graduating number is only 100 in excess of the normal demand to make up our losses; but it is well for you to remember that our population is ever increasing and that there is room in Canada, every year, for 400 additional practitioners of medicine. Putting it in other words, there is plenty of room for every man who is willing to work. The rural districts of Canada have really some cause of complaint that they are not receiving the medical services to which they are entitled. There exists to-day many a hamlet in Canada where formerly there was a doctor, in which now no practitioner is found. It has been advanced by way of explanation that the improved methods of transportation, the changed attitude of the younger men demanding hospital and laboratory facilities and more intellectual and social opportunities for themselves and their families, have kept our graduates from going to the country. Do not forget that the men who made this country what it is to-day lived on the land. At the time of Confederation 66 per cent. of the people of Canada were rural residents. This percentage has fallen to 50 in 1926. When you are ready to practice, if I may be bold enough to make a suggestion, let me say this: do not frown upon an opportunity to go to the country even if for only a few years. By so doing you will be put to the test of finding out just how much you know, and, particularly, how much you do not know. Left to your own resources, the opportunities for development, particularly the likelihood of gaining self-assurance, will be altogether to your advantage. In the

cities it is a simple matter to call in a consultant or a colleague if you feel that you are stuck. Country practice will stiffen the back-bone of any worthwhile man. Moreover, our country offers undreamed-of possibilities. In her agricultural, mining and lumbering areas, immense resources permitting of almost limitless expansion, lie before our people. But to be developed, they require the brain and brawn of man, and, where our people are found there our doctors should be ready and willing to go to do their share of work in our national development.

There is a little book published by the Canadian Medical Association which is called "The Code of Ethics." Might I suggest that you read and digest the contents of this little pamphlet carefully and often. Although it has been said that a gentleman needs no code of ethics and a man who is not a gentleman will not be bound by one, yet I feel quite certain that most of you will find this little book extremely helpful. It is divided into three chapters, namely:

1. Duties of the Doctor to the patient.
2. Duties of Doctors to one another.
3. Duties of Doctors to the Community at Large.

I have often felt that a fourth chapter might be added dealing with the duty of the public to the physician. I am forced to believe that the public to-day does not hold the profession of medicine in the same high regard that it did years ago. There are many reasons for this. With advanced civilization, we find greater opportunities for education; and, whereas the doctor, the preacher and the lawyer used to be the intelligentsia of the community, this small group of intellectuals has been augmented by a large number of the community. If the medical profession has slipped in public esteem, I do not believe it is because the profession has failed to render excellent medical service, but rather that we have failed to take the public into our confidence in

such a manner as will inspire their admiration and trust; and so I would say to you who are soon to be out in the field,—bear in mind that you have a real responsibility not only to the patient, but to the profession and the public, to do your share toward assisting the profession to enjoy that public confidence which it merits.

You should endeavour to know the rules, the plays and the signals. You will probably observe many off-sides and much interference, and the referees will not always know the rules. It will be necessary for you to acquire breadth of vision, saneness and a spirit of sport of vision, saneness and a spirit of sportsmanship which will enable you to receive rebuffs and smittings with a smile.

Like the poor, the quacks are always with us. Some of them are sincere in their beliefs. Remember that you have no quarrel with an honest effort on the part of any individual; but you have a quarrel with a State system, or lack of system, which allows any ignorant or incompetent individual to place in jeopardy the life of his fellow-man. It is your duty to use your influence in the community in which you live to insist that those who pose as practitioners of the healing art shall have at least a modern scientific training in the fundamentals of physiology and anatomy. This would prevent many ignorant charlatans from preying upon a gullible public.

As you all well know, doctors to-day give to the world eagerly and gladly the full benefit of their knowledge. Dr. Banting's discovery with its application to humanity, and the manner in which he gave the results to the world should thrill every medical man with pride. A man who invents or discovers frequently receives great material gain thereby; but not so in medicine. A story is told that sixty odd years ago, a practitioner from Ireland came out and settled in Nova Scotia, but neglected to take out a provincial license. The Provincial Registrar learning of this,

sent for the new-comer and proceeded to examine him to see if he was worthy of a license in that province. When asked what was his treatment for diphtheria, the candidate, with thumb to nose, answered, "Oh, wouldn't you like to know?" Times have changed since then.

How may a practitioner benefit from the knowledge of his colleagues? There are four avenues open to him:

1. Medical literature.
2. Contact with his confreres.
3. Attendance at post graduate centers.
4. Taking advantage of lectures and clinics through his local medical society.

Just here let me say that one of your first duties when you enter practice is to join the local medical society. During the past six years thousands of post graduate lectures have been delivered to the medical societies of Canada. They not only bring the latest information about medical progress, but they act as a great stimulus to the members. I feel so strongly as to the value of the local medical society that I am constrained to say this: if you do not consider it worthy of your support, it is not likely that you will be a successful practitioner. If the local society, in your opinion, is dull or dead, contribute your talent and liven it up. The future of medicine in Canada depends upon you, and one of the best ways you can exert your influence along the line of medical progress is through the medium of the medical society.

A thought or two about the commercial side of medicine. True it is that the laborer is worthy of his hire; but if there is one individual in the community who, more than all others, gives much without worldly reward for service rendered, it is the doctor. Charge reasonable fees according to the standards of the community in which you live. It has been estimated that the

medical profession gives a million dollars worth of free service yearly to patients in the Toronto General Hospital. One sometimes wonders if there is not something wrong with our scheme of payment. Organized medicine is today giving much thought to the whole problem of medical service. The very rich, because they can pay, and the very poor who make no attempt to pay, have little concern about the attention they receive. It is said that it is the middle class who suffer. It should not be an obligation of the medical profession to bear the cost of sickness of those who cannot pay. A happy solution of the problem yet remains to be found. Maybe some of you here will yet take part in the solution.

I have often said that if Rip Van Winkle had been a doctor he would have lost his vocation after twenty years of sleep. The honest practitioner who desires to give his patients 100% efficiency must keep himself up to date; and one is proud to tell you that the great majority of the medical profession of Canada are imbued with the sincere desire to maintain a professional efficiency in keeping with modern medical progress and thought. The practice of medicine in its relation to the public is undergoing a change. We find various groups in society studying and discussing the problem of health, constantly looking for methods which will improve the general health of the people. In the Province of Alberta, the government has instituted traveling clinics. These are available for any part of the province, and it is stated by the government that they are rendering excellent service to the people at a very low cost. The farmers of Saskatchewan, through their organization have asked the Government of the province to establish free diagnostic clinics. In practically all of the provinces of the Dominion, organizations are focussing attention on the health problem. It is very difficult to anticipate just what changes may lie before the profession in its relation to the public. Governments, either provin-

cial or federal, may one day in the not far distant future, decide to take a very definite and official interest in "the mass production of health." So long as organized medicine gives of its best and stands together, the public weal will be served and we have little to fear for the future. But we must be united if we are to take our proper place in directing health services in Canada.

A word about your future. Gentlemen, this country intrigues me with its possibilities. Although I have crossed Canada a great many times, each year I find more reasons for pride not only in our achievements, but in what I believe the future holds in store for us. Just this year that snug province of Prince Edward Island, down by the sea, with a population of approximately 87,000, exported more than fourteen million dollars worth of goods (largely potatoes and silver foxes), an amount exceeding by more than one million dollars the whole of the export trade of Canada in 1870. Our Governor-General, His Excellency Lord Willingdon, has said of Canada, "One thing that thrills me is that, in a country so large with a population so small, so much has been accomplished in a few short years." In my humble opinion,

the past is merely an index of the progress and development which we shall see during the next quarter of a century. Our potential wealth is untold. Its development depends upon two factors, namely, people and money. Canada is destined to become one of the greatest, if not the greatest country in the world, and, therefore, we, the medical profession, the watch-dogs of the health of the people, must see to it that we use our influence to have Canada populated by those who are sound in brain and body and an asset rather than a liability.

Gentlemen, you will shortly be crossing the threshold to an active career. You have a marvellous future before you. You can go to any part of Canada and find an opportunity for the fullest expression of your talents and your education. You need but three things: (1) a sound scientific training such as you are privileged to acquire at the University; (2) a sincere and proper method of approach to your fellow-men and to your task; (3) the embodiment of our code of ethics in your personality which makes you a man to be trusted. Granted you have all these, the future of Canada is safe in your hands.

***The Reticulo-Endothelial System.**

(By J. E. Bates, B.A., M.B.)

From the Department of Pathology, University of Toronto.

(Continued from December Issue).

As has been intimated, the conception of the reticulo-endothelial system is not fixed at the present time, but is in the formative stage during which all manners of functions possible and impossible, real and imaginary, are

thrust upon it. Indeed it is the fashion of the moment to suspect the reticulo-endothelial system of performing all the tasks for which the mechanism has not yet been determined. This system is unusually susceptible to such suspicion as a result of its widespread distribution in the organism. It is not the purpose of this paper to discuss all the roles ascribed to this

*Read before the Section of Pathology, Academy of Medicine, Toronto, November 22nd, 1927.

system, but rather to indicate a few of the more important functions which it is generally conceded to perform.

Blood Formation—Histiocytosis— Leukemia—Neoplasms.

The occurrence of the main depots of the reticulo-endothelial system within the hemopoietic areas suggests at once that these cells have to do with the formation of blood. Some discussion has arisen concerning the relationship of the reticulo-endothelial cells to the production of leucocytes of the granular series and even of red blood cells, but no proof of this has as yet been submitted. There are, however, a certain number of mononuclear cells containing granules of dye found in the blood of animals that have been vitally stained. From the characters of these cells they are undoubtedly derived from reticulo-endothelial elements. That is, some of the mononuclear cells in the circulating blood of normal animals are of histiocytic origin. These cells are more numerous in the venous channels and in the right side of the heart than in the peripheral circulation. In various infectious diseases they become more numerous in the blood stream and may engulf red blood cells, leucocytes, platelets, bacteria or pigment. The occurrence of malaria pigment within monocytes is widely recognized. Mallory has called attention to the increased "endothelial leucocytes" with their contained erythrocytes in cases of typhoid fever. Other conditions exhibiting histiocytosis are subacute bacterial endocarditis, septicemia, paroxysmal hemoglobinuria, typhus fever, small-pox, relapsing fever and agranulocytosis.

In addition to the histiocytosis of infectious origin, immature clasmocytes have been demonstrated in the blood in cases of myeloid and lymphatic leukemia. Whether a third type of leukemia—a true histiocytic leukemia—exists or not is a problem awaiting

further study with vital stains. Such cases have been reported, some of them showing marked localized proliferation of reticulum cells without the appearance of immature monocytes in the blood. To these the term "aleukemic reticulosis" has been applied. The suggestion has even been made that Hodgkins' disease represents an aleukemic reticulo-endotheliosis. The occurrence of primary neoplasms of the reticulo-endothelial system is difficult of proof. Endothelial tumors, such as Ewing's tumor, are known to occur in organs rich in reticulo-endothelial cells, but whether they arise from common vascular, or specialized endothelium, is not clear.

Blood Destruction—Jaundice.

While the reticulo-endothelial system plays a part in blood formation, it is much more actively concerned in the destruction and disposal of worn-out red blood cells, leucocytes, and platelets. In view of the short span of life of the red blood cell it is evident that they must undergo constant fragmentation. Whether these cells fragment in the blood stream with subsequent phagocytosis of the hemoglobin-containing particles, as occurs in normal animals; or whether the red blood cells are engulfed bodily as in various pathological conditions, the reticulo-endothelial cells of the spleen, bone marrow and liver form the mechanism for their disposal. Under normal conditions the spleen appears to be the chief site of erythrocyte destruction, but if it be removed the reticulo-endothelial cells of the liver, bone marrow, and lymph nodes proliferate and take over its functions. The increased erythrophagocytosis observed in typhoid fever, typhus exanthematicus, malaria and other acute infectious diseases is probably the result of a primary damage to the red blood cells with a consequent increased demand upon the reticulo-endothelial cells. In Weils' disease the red blood cells appear to undergo preliminary erythrorrhesis

with subsequent phagocytosis of the resulting fragments.

While in infectious diseases the entire reticulo-endothelial system takes part, it is interesting to note that in the hemolytic anemias a selective phagocytosis occurs. Thus in pernicious anemia the phagocytosis occurs mainly in the bone marrow. Indeed there is much reason to believe that many of the newly formed nucleated red cells are phagocyted by clasmatocytes within the bone marrow without ever having gained entrance to the blood stream. On the other hand in hemolytic jaundice the greater part of the phagocytosis is accomplished in the spleen and not infrequently removal of the spleen is beneficial.

Little is known regarding the final disposal of the leucocytes of the blood stream in view of the fact that their products of disintegration are non-pigmented. The same holds true for platelet destruction, but in this instance a certain amount of knowledge has been gained from observations on experimental animals and on cases of thrombocytopenic purpura. The cause of this latter condition appears to be an excessive destruction of platelets occurring in the spleen. In many of these cases the haemorrhages cease and the platelet count rises to normal subsequent to splenectomy. A complete cure may be obtained provided that the remaining cells of the reticulo-endothelium do not assume the abnormal function of those within the spleen. The work on experimental animals has been very interesting in that splenectomy in a normal animal causes a marked rise in the platelet count with a subsequent sharp fall as the remaining cells of the reticulo-endothelial system compensate for the loss of the cells removed with the spleen. Intravenous injections of India ink to "block" the physiological functioning of the reticulo-endothelial cells causes an approximately similar increase in platelets. It has been found impossible to superimpose the rise in plate-

lets following splenectomy upon the rise produced by a previous "block." In such "blocked" animals the entire reticulo-endothelial system has been temporarily affected, so that the removal of a part of this paralyzed system produces no further effect. It was, however, possible to cause a rise in platelet count by blocking the reticulo-endothelial system of an animal after it had recovered from a previous splenectomy. This does not by any means represent the whole story in connection with the maintenance of the platelet level because the presence of the spleen in the body may inhibit the formation of platelets rather than contribute to their destruction. It is also evident that some other mechanism than the reticulo-endothelial system must be concerned in platelet destruction, else repeated "block" of these cells would lead to an increase in the platelet count ad infinitum.

The consideration of the mechanism for scavenging the worn out red blood cells raises the problem of the site of formation of bile pigment. It has long been known that hematoidin and bilirubin are isomers, and that the breaking down of hemoglobin provides the material from which bilirubin is formed. Because of the inability to produce jaundice in dehepatized birds it was believed for many years that the parenchymal cells of the liver were essential to the production of bile pigment. The first step in the elucidation of this problem was a recognition of the fact that in birds the main site of the reticulo-endothelial system lay in the liver, and was of necessity removed along with it. It has been known for some time that bilirubin is formed in old hematomata, and it now appears that the histiocytes, which phagocytose the red blood cells, are responsible for the appearance of this pigment. In the last few years much work has been undertaken to prove an extra-hepatic origin of bilirubin. Investigations have been carried on from a number of angles, but it would be impossible to

deal with them in detail in this paper. By means of saturating the reticulo-endothelial system with collargol it has been found possible to minimize, if not actually to eliminate, the jaundice resulting in birds treated by arseniuretted hydrogen. It has been abundantly proven that bilirubin accumulates quite rapidly in the blood serum of dogs within a few hours after complete removal of the liver and that the rate of its accumulation is not affected by a simultaneous removal of the spleen, or of all the abdominal organs, providing that circulation to the extremities is maintained. It has also been shown that the venous blood returning from the bone marrow, spleen and liver, contains more bilirubin as estimated by the spectrophotometer than does the arterial blood. Moreover, perfusion of the spleen with laked red blood cells results in the appearance of bilirubin in the perfusate. Thus bilirubin is quite definitely formed in organs rich in reticulo-endothelial tissue and it is becoming increasingly clear that the only function of the liver cells in respect to bile pigment is to excrete it, at the same time perhaps altering it by the addition of some of the other constituents that go to form bile. In the light of this knowledge it would appear that the liver cells behave toward bilirubin in much the same way that the kidney cells do to urea, and that they maintain the bilirubin in the plasma at a constant level. It is interesting to note that amounts of bilirubin, too small to be detected by chemical means, may be demonstrated in normal plasma by the spectrophotometer.

Metabolic Functions—Iron—Lipoids.

In addition to the formation of bilirubin from the breaking down of red blood cells the reticulo-endothelial cells attempt to store the iron-containing fragment so that it may be utilized again. Little is known of the final disposal of this pigment. It is not surprising that the spleen, which is one

of the main depots of the reticulo-endothelial system and in which there is much breaking down of red blood cells, is intimately concerned in the metabolism of iron. Following splenectomy, both in experimental animals and in the human, there is a great increase in the renal excretion of iron and there is an increased iron infiltration of the Kupffer cells. Hemosiderin has also been observed within the reticulo-endothelial cells in the later stages of such infectious diseases as are characterized by the phagocytosis of red blood cells. In states of hunger and inanition the reticulo-endothelial cells contain much iron. In pernicious anemia the greatest amount of hemosiderin is found in the bone marrow. The spleen contains but small amounts of iron and it appears that the splenic domain of the reticulo-endothelial system has refused to function. This paucity of iron in the spleen is in keeping with the small amount of phagocytosis occurring there. In toxic hemolytic jaundice other factors are brought into play and the iron deposit in the spleen is more pronounced. In hemochromatosis enormous amounts of iron containing pigment are found as coarse granules in the reticulo-endothelial cells of the liver and in the retroperitoneal lymph nodes as well as in the parenchymatous cells of many organs. The nature of this disease is puzzling because apart from a mild anemia, signs of increased blood destruction are wanting. It is suggested that the accumulation of the iron in this disease is due to a functional insufficiency of the reticulo-endothelial cells in handling the iron liberated from the blood at a normal rate with its consequent storage in the parenchymatous cells of various organs.

The cells of the reticulo-endothelial system present a great affinity for lipoids. They are not infrequently found in the walls of old abscesses, or pus tubes, in atheromatous plaques of the aorta or in chronic mastitis where

they have taken up the fat set free from disintegrating cells. Localized infiltrations of lipoid laden histiocytes, forming tumor-like proliferations in the form of xanthomata, occur in association with hypercholesterolemia or lipemia. The Kupffer cells of the liver are especially prone to store up fat in diabetes, but the histiocytes of the spleen may also take up so much that splenomegaly results. In Gaucher's splenomegaly, one recognizes a system disease of the reticulo-endothelial apparatus associated with some disturbance of lipoid metabolism. Instead of leading to a deposition of fat or cholesterol in the reticulo-endothelial cells, one finds large amounts of a phosphorous containing cerebroside with the chemical properties of kersin. The Gaucher cells are limited to the hemopoietic organs and are most numerous in the spleen, where they are derived chiefly from the reticulum cells which contain much less iron than the endothelial cells lining the venous sinuses.

Inflammation — Phagocytosis — Immunity — Repair.

The reticulo-endothelial cells play a very special part in clearing the system of inert foreign bodies, as, for instance, carbon. The removal and storage of such substances are accomplished mainly through the activity of the histiocytes. These carbon-laden cells may best be seen in the lungs and peribronchial lymph nodes and are particularly numerous in oedema of these tissues.

The participation of cells of the reticulo-endothelial system in the response to injury has long been recognized, but recent studies are adding a deeper significance and a wider knowledge to the part taken by these cells. It is quite clear that the histiocytes act as scavengers, clearing up the cellular and bacterial debris from local areas of inflammation. They are active in the healing of fractures, rounding off sharp spicules and eroding Haversian

canals in the newly-formed bone. Recent studies have demonstrated that pure cultures of monocytes may be transformed into fibroblasts under certain definite circumstances, so that it becomes apparent that these cells may at times aid very directly in repair by fibrosis.

In ordinary infections these cells participate by phagocytosis and intracellular destruction of the microorganisms whether they be bacteria or protozoa; by ingestion and disintegration of red blood cells; by proliferation and entrance to the blood stream; and probably by the absorption of soluble toxins and the secretion of antibodies. The phagocytosis of bacteria by reticulo-endothelial cells occurring in man in spontaneous disease, is much less prominent than that seen in experimental animals where large amounts of bacteria are injected intravenously or especially where immunized animals are used.

The most marked reaction of the reticulo-endothelial cells is found in typhoid fever where they actively phagocyte red blood cells and cellular debris, but do not contain bacteria. In other conditions such as paratyphoid, subacute bacterial endocarditis, septicemia, smallpox, malaria, Kala-azar, trypanosomiasis, Rocky mountain spotted fever, typhus fever, measles and cholera, actively phagocytic cells are observed.

Whereas the phagocytosis of microorganisms is usually regarded as a defensive reaction, it is not unlikely that in some instances it may represent a symbiosis between the micro-organism and the engulfing cell. The question of symbiosis is particularly relevant to the consideration of leprosy, tuberculosis and other granulomata where the engulfed micro-organisms may remain viable over long periods of time. Studies with vital dyes have shown that histiocytes are the essential cells in many specific granulomata, especially in tuberculosis, leprosy, blastomy-

cosis and sporotrichosis, but also in others. In tuberculosis, both monocytes and clasmatoocytes are found to play their part. The epithelioid cells, which predominate in these lesions, are thought to be derived from the monocytes which are of reticular origin. The giant cells are thought to be derived from the same source and the peripheral arrangement of their nuclei is explained by the central position of the hypertrophied (monocytic) rosette. These cells of monocytic origin may be observed to retain the tubercle bacilli apparently uninjured, while on the other hand the few clasmatoocytes present in the lesion bring about disintegration of the contained bacilli. The large cells occurring in Hodgkins' disease are believed to be of similar origin. The striking feature about the granulomata is that while the cells in all have a similar origin they exhibit special cell alterations which are characteristic of each. Thus tubercle formation is characterized by fibrillar intercellular substance and giant cells; the lepra node by bacilli laden cells; the sporotrichoma by peculiar lipid cells; leishmaniosis by swollen, parasite-containing cells; and actinomycosis by characteristic local suppuration about the colonies.

As I have already indicated, Metchnikoff attributed to his macrophage system the power to produce hemolysins, agglutinins and coagulins. While the question is still an open one, experiments on various animals are highly suggestive that such is the case. Unfortunately no direct evidence in this regard is forthcoming from a study of pathologic conditions in man. It has been shown that foreign red blood cells introduced into the circulation of rabbits are destroyed chiefly in the spleen, liver and bone marrow. Also extraction methods have demonstrated that tissues rich in reticulo-endothelial cells are also rich in antibody content. Indeed hemolysins have been produced *in vitro* by the addition of foreign erythrocytes to cul-

tures of bone marrow. The greater part of our information regarding the role of the reticulo-endothelial system in immune reactions has been obtained through experiments designed to nullify or lessen the functional activity of this system by means of splenectomy; or of saturating the cells with various dyes or inert particles; or by a combination of both methods. In view of the varying inter-relationships of the different domains of the reticulo-endothelial cells in different animals it is evident that there are serious objections to the application to the human of the conclusions reached by this type of experiment. In general, however, it has been found that there is a reduction in antibody production, and a suppression of the production of antitoxin in animals previously subjected to repeated intravenous administration of dye stuffs. The immune response of tuberculous animals to tuberculin has also been lessened by similar injections of dye. Conversely it has been shown that animals which have been immunized against certain vaccines lose the power to store vital dyes. The failure of some experimenters to corroborate these results may be due to an insufficient dosage of the blocking dye or to failure to establish a block because of the rapid cleaning and regeneration of this system by the continual shedding of its cells into the circulation.

Not only do the reticulo-endothelial cells appear to play a part in general immunity, but the histiocytes resident in the fixed tissues modify local reactions as well. The intracutaneous response to vaccinia in the rabbit may be reduced or abolished if the virus is inoculated with, or subsequent to, an injection of India ink of sufficient concentration. It has also been shown that the resistance of the peritoneum to bacterial infection is increased when the exudate is rich in macrophages. Such a proliferation of the tissue histiocytes may be brought about by intra-peritoneal injections of olive oil.

Conclusion.

Out of the multiplicity of functions ascribed to the reticulo-endothelial system, it would appear that the chief functions concerned are, first, with blood formation or the presence of certain of the mononuclear cells within the circulation; secondly, with blood destruction both in regard to red blood cells with a consequent formation of bilirubin, and to the disposal of the platelets; thirdly, in the metabolism of iron and lipoids; and fourthly, with the various phases of inflammation and repair.

In view of its participation in the performance of these important functions, it is not surprising that attempts have been made to influence the activity of this system by therapeutic measures. This is a field offering a wide scope of usefulness, but on account of the diversity of functions which may be so modified, great care must be exercised. A temporary diminution of function may be obtained by splenectomy, and if the remainder of the reticulo-endothelial system does not proliferate to take over its function, the diminution may remain permanently. It is claimed that if the reticulo-endothelium is blocked with colloidal silver, various drugs and antiseptics will

remain in the circulation over longer periods of time. Certain drugs, such as morphia, atropine and pituitrin, are said to decrease the activity of the cells of this system. On the other hand the activity is said to be increased by pilocarpine and by the injection of various colloidal substances, especially proteins. On this account it has been suggested that the efficiency of non-specific protein therapy depends upon the activity of the histiocytes. Weak dosages of roentgen ray appear to stimulate the histiocytes, while large dosages paralyze them. The problem of the therapeutics of reticulo-endothelial cell dyscrasias is alluring, but is very complex, and at the present time has barely reached the experimental stage.

References.

- Full references may be found in:
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THE BACTERIOLOGICAL BALL.

A gay bacillus, to gain her glory,
Once gave a ball in a laboratory.
The fete took place on a cover glass
Where vulgar germs could not harass.
None but the cultured were invited,
For Microbe Chicks are well united.
They closely shut the ball-room doors
To all the germs containing spores.
The Staphylococci first arrived,
To stand in groups they all contrived.
The diplococci came in view
A trifle late and two by two.
The streptococci took great pains
To seat themselves in graceful chains.
The pneumococci, stern and haughty,

Declared the gonococci naughty
And said they would not come at all
If the gonos were present at the ball.
The fete began, the mirth ran high
With not a fear of danger nigh.
Each germ enjoyed himself that night
Without a fear of phagocyte.
'Twas getting late and some were
loaded,
When bang!! the formaldehyde exploded;
And drenched that happy dancing mass
That swarmed the fated cover-glass.
Not one survived, but perished all
At that bacteriologic ball.

*Anemias.

By K. G. Gray, 2T8.

It is the purpose of this paper to arrive at a method of classifying anemias, rather than merely to string off the orthodox classification. It is an attempt to appreciate the way of assembling the evidence which leads one to place an anemia in a given group. Nothing in the paper is original: the sources are acknowledged elsewhere. From these sources a new viewpoint was experienced on the subject, a viewpoint which is stimulating, productive, dynamic. The method of these hematologists seems so valuable that we have taken the liberty of summarizing it.

The plan of the paper embraces: (1) The hemopoietic system. (2) Some facts about blood destruction. (3) A classification of anemias, especially as regards the reasons for placing an anemia in a given class.

The Hemopoietic System, or the Blood Corpuscles and their Formation. They consist of three main types: red, white and third corpuscles (or platelets or thrombocytes).

The Red Blood Cells. The reds are very flexible, non-nucleated cells, whose normal form is a biconcave disc. Roulleaux and crenation are without pathological significance. With the method of vital staining, blue staining, finely granular filaments or a small network of filaments, the "substantia granulofilamentosa" appear in less than one per cent. of the cells. These are the cells usually known as the reticulated reds. Average diameter of the red blood corpuscles is 7.5 microns. The cells stain with acid dyes and not with basic, when a mixture of the two is applied to them, a phenomenon known as orthochromasia, and is dependent upon a normal Hemoglobin content. When the Hemoglobin is diminished, the cells tend to become basophilic. Normal cells show

a central achromia, because the centre of the cell is thinner. The normal count in the male is about 5,000,000; in the female, 4,500,000.

The White Blood Cells. The white cells comprise the granular leucocytes (polymorphonuclear, neutrophiles, eosinophiles and basophiles); the mononuclear leucocytes (also known as the transitional cells of Ehrlich, or endothelial cells); and the lymphocytes.

The Platelets. The platelets are anuclear, rounded irregular masses, staining a hyaline blue with purplish granules. Within the vessels of the living animal, platelets occur singly. Immediately on leaving the vessels, they tend to stick together in groups. The normal count is 250,000 to 350,000 per cubic mm.

Oxydase is present in granular leucocytes and mononuclears but not in lymphocytes, red cells or platelets.

Formation of the Cells.

The red blood cells, granular leucocytes and platelets are normally formed out of cells of the red marrow of bones and are not capable of reproducing themselves. In adult life, the marrow in long bones becomes largely fat tissue and the red marrow is restricted to the flat bones.

Within the marrow, are proceeding three generic systems, terminating respectively in the red cell, the granular leucocyte and in the platelet.

There is the generic system of erythroblast, to red cell. Secondary, myeloblast, to myelocyte, to leucocyte. Thirdly, the platelets are formed by extrusion of portions of cytoplasm from the megakaryocyte. Hence, in the marrow, at any time, we have a great variety of cells, some of which are mature and find their way into the circulation, others which are immature and are confined to the marrow. The question aris-

* A paper read before the "Eighth Club," Nov., 1927.

es, why do only the mature cells reach the circulation? What is the process by which the formed or adult cells are filtered out and carried off in the blood stream, whereas the immature cells are left behind in the hemopoietic areas? To cover this point the hypothesis has been advanced that the endothelial lining of the vessels in the marrow is of a special type, permeable to the mature cells and offering a barrier to the immature cells. Hence, if immature cells appear in the circulation it implies not only stimulation of the erythrocytic centres but a damaging of the endothelial barrier.

The origin of the mononuclears or endothelial cells is not known.

In the embryo, the earliest blood cells are derived from the yolk-sac and are known as megaloblasts. Erythrocytic function is next assumed by the liver and spleen; in the later months of embryonic life, the function, as in the adult, devolves upon the bone-marrow. In adult life, under normal conditions, megaloblasts are found nowhere in the body.

Summarizing the facts about cell formation, we have:—

From bone marrow: red cells, granular leucocytes, platelets.

From lymphatic tissue: lymphocytes.

Of unknown origin: endothelial cells, An embryonic type, the megaloblast, appearing only in disease.

Abnormalities in the Red Blood Cells.

Below are listed the common deviations: For explanation consult the references.

Anisochromia.

Anisocytosis.

Poikilocytosis.

Nucleated cells.

Howell Jolly bodies.

Cabot's ring bodies.

Increase in reticulated cells.

Polychromasia.

Stippling.

Blood Destruction.

The metabolism of red blood cells involves genesis in the marrow of flat bones, destruction and bilirubin forma-

tion in the reticulo-endothelial system, and excretion of bile pigment at the liver. The formation of the cells has been considered; we are now in a position to consider the destruction and disposition of them.

If all bile pigment be assumed to have formed from hemoglobin, the daily destruction of red cells may be estimated at one-tenth to one-fifteenth of the total blood.

Hemolysis plays little part in the destruction. Fragmentation is the predominant factor in initiating the process.

Role of the Spleen. The actual site of red cell destruction is not known, but the spleen plays some part in preparing the cells for disintegration. This is known as Bottazzi's hemocatatonic theory of splenic function. Splenectomy in a normal animal causes:

Increased resistance of the red cells to hemolytic agents.

Decreased bile pigment excretion.

From this it may be argued that the removal of the spleen decreases red cell destruction.

Banti's hypothesis is that the spleen normally furnishes a substance which acts on the cells and prepares them for destruction. This view is the basis for splenectomy in the treatment of anemias.

A consideration of blood destruction really carries us into the field of bile pigment formation. Bilirubinogenesis is the natural sequel to the story of hemolysis.

Bilirubin is iron-free hematin, formed from hemoglobin in the reticulo-endothelial system. There are two types of bilirubin.

The first type, blood serum bilirubin, is normally present in the blood up to 0.5 units. It is never excreted in the urine as bilirubin, but is changed to urobilin. It is combined with protein in the blood serum, hence gives an *indirect* Van denBergh reaction. Urobilin and blood serum bilirubin are increased whenever there is increased hemolysis.

The second type, bile capillary bilirubin, is not found in normal blood. It

is formed from serum bilirubin which has passed through the liver cell into the bile capillary. It is excreted unchanged in the urine. It exists free in blood serum, giving *direct* Van denBergh. It is increased whenever the bile passages are obstructed.

Hence, in increased hemolysis, the blood serum gives an indirect Van denBergh reaction; a fresh sample of urine, tested with Ehrlich's reagent, shows presence of urobilin. The stools are dark, because of increased stercobilin. In Pernicious Anemia, there is a direct Van denBergh, indicating resorption of bile capillary bilirubin: possibly the bile capillaries are plugged because of the excessive production of bile pigment.

In the dynamic view of hematology, certain signs which appear on clinical and laboratory examination are interpreted in terms of an alteration in the function of the mechanism which controls blood formation, destruction, and excretion. Some of these signs and their meaning may be grouped with advantage, at this point.

Signs of Stimulation in the Bone Marrow.

Leucocytosis.—This affects the granular leucocytes, so that there may be a relative decrease in lymphocytes.

Increase in the platelets.

Increase in the reticulated reds.

The stimulation may proceed to a point where the marrow becomes pathological, setting free abnormal cells:

Polychromasia.

Stippling.

Nucleated reds.

Megaloblasts.

Signs of Depression of the Bone Marrow.

Thrombocytopenia: decrease in platelets.

Leucopenia.—This affects the granular leucocytes so that there may be a relative lymphocytosis.

Absence of the signs of regeneration in the smear.

Urobilin and Van denBergh negative.

Signs of Increased Blood Destruction.

Increase of the urobilin index of the urine.

Positive Van denBergh.

Smear shows the signs of stimulation of the bone marrow, given above.

Stools dark, because of increased stercobilin.

Classification of Anemias.

Anemia is defined as a condition in which there is reduction of the oxygen carrying constituent of the blood, namely hemoglobin. This is usually associated with reduction of red blood cells. It is customary to regard an appropriate blood picture as sufficient evidence of anemia, even though there is no reduction of hemoglobin and hence, technically, no anemia.

Anemias are classed according to the method of production. Classification is complicated by the fact that, in some anemias, more than one method of production is operative, while in others the method of production is not known.

Classes of Anemia.

1. Due to mechanical loss of blood.
2. Due to defective or inadequate blood formation.
3. Reduction in blood formation.
4. Increased blood destruction.

1. Anemias Due to Mechanical Loss of Blood.

(a) Due to acute blood loss.

If more than one-third of the total blood be removed suddenly, death ensues. Up to two-thirds of the total blood may be removed slowly (gradually over a period of twenty-four hours). Reduction of the hemoglobin to less than one-quarter of the total amount is incompatible with life.

An example of this type of anemia is the condition of a donor after transfusion.

Examination of the blood immediately after loss of blood, shows all readings normal.

Within a few hours, leucocytosis, increase in platelets and increase in re-

ticulated red cells appear. For a few hours, the red count and hemoglobin are normal. Then dilution of the blood begins; red count and hemoglobin fall. The rate of dilution depends upon the fact that nature will not reduce the hemoglobin below thirty per cent. The maximum dilution occurs in two to three weeks. At this time, the relative anemia is greatest, but the absolute anemia is diminished and the patient is well on the road to recovery. Red cell formation is more rapid than hemoglobin production, so that achromia occurs. Symptoms in this type of anemia are due, not to the anemia, but to the reduction in blood volume.

(b) Anemia due to chronic blood loss.

This type occurs in hemorrhoids, gastric and duodenal ulcer, fibroids, hepatic cirrhosis, etc. The blood picture varies, depending upon duration of the blood loss, total amount of blood lost, and the response of the bone marrow.

When the marrow is responding actively, we have the signs of marrow stimulation.

After a prolonged, chronic blood loss, the bone marrow will not respond so actively: there will be less leucocytosis, less increase in platelets, less increase in reticulated reds.

As hemorrhage continues, the marrow may show less and less response, resulting finally in a leukopenia, or a diminution in reticulated reds. Thrombocytopenia from this cause is rare. A condition of true aplasia from blood loss does not occur.

The diagnosis of chronic hemorrhagic anemia is usually easy. There is a history of blood loss. The blood picture is one of anemia plus bone marrow stimulation. It is only the relatively rare types with depression of the bone marrow that may be confused with Pernicious Anemia.

2. Defective or Inadequate Blood Formation.

In general, this includes that group of anemias which are commonly secondary. It is usually easy to find the primary disturbance which is causing the

anemia, or has, with it, a common etiology. The anemias of cancer, tuberculosis, nephritis and lead poisoning are classified as due to defective formation.

The hypothesis held for this group is that for some reason which is not clear, there is interference with the normal, orderly delivery from the bone marrow to the circulating blood of the types of cells seen in health.

The typical picture is the same as for chronic blood loss:

Reduced red cell count.

Reduced hemoglobin.

Color index less than 1.

Smear shows signs of slight bone marrow stimulation, with achromia of red cells.

In severe cases, the smear may show macrocytes, leucopenia, diminished platelets, and cells not normally present. The color index may be about 1.0, and it may be difficult to differentiate Pernicious Anemias.

Chlorosis is a special type of anemia due to defective formation. It is largely a clinical entity of unknown cause. It is a slow disease with tendency to spontaneous cure. It occurs exclusively in young women, aged 14 to 25 years. The condition is gradually disappearing in this generation. It is generally associated with faulty hygiene: constipation, tight lacing, excessive eating of candy. Although considered due to abnormal iron metabolism, there is no evidence of blood destruction. The red cells are reduced, but the most marked reduction is in hemoglobin, so that the cells show marked achromia. Leucocytes are normal; there is no increase in reticulated reds; platelets increased. In marked cases there is a typical green color of the skin.

3. Reduction in Blood Formation, or Quantitative Alteration in the Function of the Bone Marrow.

We have just finished discussing the anemias due to blood loss and those produced by a defective functioning of the bone marrow. At times, instead of suggesting a deviation from the normal function, the picture is one of lack of

function of varying degree, a condition designated as depression of the bone marrow. Bone marrow depression may occur as a phase in any anemia due to defective function. It is also found in Banti's disease, occasionally in Pernicious Anemia, and in certain hemolytic anemias. There are certain other conditions in which the blood picture of a depression of the bone marrow is associated with an actual reduction of hemopoietic tissue in the bone marrow. Some of these are called aplastic anemias, which may be of any grade. The replacement of hemopoietic areas by tumors, etc., will be discussed under the heading of Myelophthisic Anemias. Benzol, radium, roentgen rays, trinitrotoluol, and certain infections e.g. typhoid, may produce partial or even complete aplasia. In addition to these secondary aplastic anemias, there is one form of unknown cause, known as idiopathic aplastic anemia.

The blood picture shows a depression of the bone marrow, as evidenced by thrombocytopenia, leukopenia, no rise in urobilin or Van den Bergh, and absence of the signs of regeneration.

The thrombocytopenia is associated with prolonged bleeding time, and a non-retractile clot.

The red cells and hemoglobin are reduced proportionately so that there is little change in the appearance of the cells.

Myelophthisic Anemia.

This term implies the anemias due to replacement of the hemopoietic tissue by tumors or tumor-like formations. The involvement must be extensive to have any effect.

The causes are:

Metastatic tumors, such as hypernephroma, cancer of breast or prostate.

Osteosclerosis.

Primary bone tumors, e.g., myeloma, chloroma.

The crowding out of erythrogenic areas occurs most typically in myelogenous leukemia; it occurs also in lymphatic leukemia.

The blood picture is variable. Early, one finds the signs of stimulation of the bone marrow. Later, the signs of depression occur. In myelogenous leukemia, there is increase in the white blood cells and platelets. In lymphatic leukemia there is a polymorphonuclear leukopenia, diminished platelets, and a diminished red cell count.

4. Hemolytic Anemias.

In this group one finds the signs of hemolysis, usually with signs of stimulation of the bone marrow. Later, there may be signs of depression of the bone marrow.

The chief causes are:

Chemical poisons: Coal tar derivatives, potassium chlorate, arsenuretted hydrogen, T.N.T.

Anemias in acute infections, such as septicemia, malaria. Pregnancy and the Puerperium. An anemia may arise during pregnancy, due to the pregnancy and not to associated hemorrhage. It is classed with the toxemias of pregnancy.

There is a cryptogenic group, of unknown cause.

Splenic Anemias.

This term includes certain clinical types where there is hemolytic anemia plus splenomegaly. The most notable are: Banti's disease, Gaucher's disease, hemolytic jaundice. It does not include: Pernicious anemia, anemia of Dibo-thriocephalus latus, portal thrombosis, Hodgkin's disease, cirrhosis of the liver, syphilis, malaria—although in all these diseases there is splenomegaly and hemolytic anemia.

Addison's Pernicious Anemia.

This disease is considered apart, because of the difficulty of classification, and because it is such a definite clinical entity of which the anemia is only one phase. It may be assumed to be a toxemia involving the blood, the central nervous system and the gastro-intestinal tract.

As regards the anemia, in what class should it be placed? It exhibits the

signs of blood destruction: elevation of the urobilin index, positive Van den Bergh, lemon color of the skin, and signs of regeneration in the smear. It shows certain signs of bone marrow stimulation: increase in reticulated reds. The signs of a pathological bone marrow are present: immature cells, poorly formed cells, megaloblasts may be found in the circulation. There is evidence of depression of the bone marrow: thrombocytopenia and leukopenia.

Pernicious anemia is generally considered as one of the hemolytic group.

For the sake of clarity, we have presented the various classes of anemias as

rather well demarcated pictures. In the majority of cases this obtains, but a large group remains in which the diagnosis is complicated by the signs of more than one method of production. In all cases, however, it is of more value to attempt to correlate the findings with the underlying pathologic physiology—which is the essence of this viewpoint.

The viewpoint expressed in this paper has been obtained from Nelson's System of Medicine; the lectures of Prof. Duncan Graham; and from Mackay and Walker, "Jaundice," in the University of Toronto Medical Journal, 1925.

Automobile Accidents Affecting Children.

By Dorothy J. McCullough, M.A., 2T8.

A glance at the morning papers is sufficient evidence to show that motor accidents play a large part in the injuries and fatalities of children. From statistical records of Toronto from 1921 to 1925 inclusive there were 77 fatalities between the ages of 1 to 14 years and this was 45 per cent. of the fatalities due to the same cause of all ages. From 1921 there has been a gradual increase in the number of fatalities of children due to motor cars. It was also noted that children between the ages of 5 and 9 years topped the list and that boys figured more than girls.

Minor Wounds.

In all cases of open wounds due to motor accidents an intramuscular injection of 1,000 units of antitetanic serum must never be overlooked. Minor wounds, due to motor accidents in children, are not so frequent as severe wounds. These take the form of lacerations or contusions. It must be remembered that the majority of accidents happen to children of the poorer classes who are left to romp about at large and as one doctor puts it "Are apt to find their pleasures in pursuits of doubtful cleanliness." Hence a minor in-

jury after being cleansed with any simple remedy like 2.5 percent iodine or alcohol must be protected and in such a way as not to interfere with the child's freedom. Collodion, "new skin" or one of the surgical varnishes such as "mastidol" may be used.

Severe Wounds.

A severe wound coming under the doctor's care within twenty-four hours of the accident is treated by simple excision and primary suture. This is especially advisable in such sites as the scalp and the extremities. This procedure may be adopted as it has been shown that during this space of time infection does not pass to any great depth in the walls of the wound. First of all stop any haemorrhage, then cover the wound and if necessary shave the immediate area. The next step is to clean up with gasoline, iodine and alcohol. A tourniquet may be applied to give one a dry field, if applicable and necessary. Now look for cut tendons, injured vessels, foreign bodies and if a scalp wound, for fissured or depressed fractures. The wound tract is excised under an anaesthetic. Cut tendons or nerves are sutured end to end. The

wound surfaces are dried with alcohol and the deep tissues are closed with interrupted sutures. The skin edges are then approximated with interrupted dermal sutures or Michel clips, leaving one point for drainage. This method is particularly applicable to hospital cases as it lessens the time of the child's stay in the hospital and does away with the changing of dressings which is painful. Another method of treatment is to clean up the surrounding tissue, wipe out the wound with some simple antiseptic as iodine, sew up the wound, put on a moist dressing and have the patient returned to the doctor daily till healing is established. It is rare to have suppuration with such treatment.

Middle Meningeal Haemorrhage.

If a fissured fracture has torn a middle meningeal artery, the history of symptoms is fairly typical. There is a history of the child being struck by a car and either becoming unconscious or dazed from concussion for perhaps a few minutes and following that a lucid interval. The latter may be very brief but usually occurs due to the fact that it takes some time for the blood to separate the dura from the skull. After this interval the child becomes unconscious again and shows signs of compression due to the extra dural haemorrhage pressing upon the brain. This likely causes anaemia of the medulla stimulating the vital centres, causing a rise in blood-pressure, a slow full pulse and blowing, continuous, stertorous respirations. This condition if not relieved goes on to a fall in blood-pressure, a rapid pulse and loud rapid respirations, to failure of the respiratory centre and then failure of the heart. The cerebrospinal fluid pressure is greatly increased. Most cases show some blood present indicating actual brain damage. If there is very much blood the danger is grave, and it means an extensive subdural injury besides the extra dural haemorrhage. There are certain lateralizing signs which if any of them are present are of value in operating on a case of this kind; a scalp wound on the

side of the lesion, a fissured fracture on the side of the lesion, as shown by X-ray plates, pupil on the side of the lesion large and fixed due to paralysis of the third nerve, some motor rolandic signs on the opposite side from the lesion.

The treatment is immediate operation. The procedure is to make a three-inch vertical incision through the skin and subcutaneous tissues from the top of the zygoma about three-quarters of an inch in front of the ear. Put in a mastoid retractor and split the temporal muscle. Remove a small button of bone. If there is no underlying clot close up the wound and proceed to the other side and do the same thing. If a clot is found enlarge the opening in the bone to two inches. Locate the bleeding point and ligate it or put on a "Cushing" silver clip. If the bleeding point cannot be located put in some light packing till the patient can be removed to a place where better facilities for working can be had.

Nerve Injury in Fissured Fractures.

Besides vessels being injured by a fissured fracture a nerve may be injured by the direct trauma or by haemorrhage. For example, the facial nerve is the one most often involved. If facial nerve paralysis comes on at the time of the accident it is likely due to haemorrhage and is serious. If however it does not appear until the third or fourth day it is likely due to a little inflammation which will clear up. If meningitis, it doesn't come on until around the tenth day and is always fatal.

Depressed Fracture of the Skull.

The other indication for operation on a fractured skull is depressed fracture. When there is no symptom of compression there is no urgent need for operation for three or four days but it is advisable in all cases to re-elevate the bone, because later in life the patient is likely to suffer from signs of pressure if this is not carried out. A depressed fracture with signs of compression should be operated upon at once unless the child is dying. If this is

not carried out failure of the respiratory centre will result. In re-elevating, if the bone has any preiosteal attachment leave it, if not remove it and the space will fill in with dense fibrous tissue.

Compound Fractures of the Skull.

Compound fractures of the skull are not operated upon unless for a depressed fracture. The child is kept absolutely quiet in bed on a Bradford frame with a binder around the chest to prevent tossing. He is kept warm and normal function is regulated. If the fracture is of the posterior fossa the blood will show on the scalp, if the middle fossa bleeding will occur from the nasopharynx and the patient will swallow the blood and vomit it. Involvement of either the middle or anterior fossae will cause tearing of the orbital periosteum and subconjunctival haemorrhage will appear within twenty-four hours. A fissured fracture involving the middle ear and drum will cause bleeding from the ear and the danger here is from infection. When the bleeding lets up a little cleanse the external canal with a one in a thousand solution of bichloride of mercury or alcohol and insert loosely some cotton soaked in one of these solutions and change every hour. Cases of subdural damage require much more rest than those of extra-dural damage. The length of time to keep a child in bed after a compound fracture of the skull depends entirely on the severity of the injury. Children seem to recover from fractured skulls extremely well.

Fractures of the Extremities.

Fractures of the extremities are quite often met with as the result of motor accidents to children. At the children's hospital they report more broken legs than arms and frequently both femurs are fractured. The diagnosis of a fracture is made on the history, signs of local trauma, deformity, crepitus, preternatural mobility and loss of function. Of course all these signs may not be present.

In children fractures of the femur occur in the middle third. A simple frac-

ture of the femur is treated without an anaesthetic. A Buck's extension is applied to the leg and fastened to the end of a Thomas' splint in which the leg is suspended. The splint is attached to the foot of the bed and the latter is elevated so that the weight of the child acts as a counter-extension.

Fractures of the shaft of the tibia are best put up in circular plaster from well above the knee to the toes with the knee slightly flexed and the foot plantar flexed. In three weeks remove this plaster, straighten out the knee and put the foot at right angles to the shaft and again put in a circular plaster until firm bony union is established. Fractures of the tibia in children unite much more readily than in adults.

In dealing with a compound fracture there are several things to remember. Antitetanic serum should be given. Measures should be taken to arrest haemorrhage. If it is arterial haemorrhage put on a clamp and later ligate the vessel. Do not use packing as there is danger of infection. Have an x-ray taken. Test for nerve lesions. Then pain must be relieved. If it is necessary to apply a tourniquet never put one on below the knee or the elbow because they won't compress the blood-vessels since in these locations they are protected from compression by the bones. Place the tourniquet high up in the arm to avoid pressure on the musculo-spiral nerve and well up in the thigh to avoid the synovial pouch of the knee and remember that two hours is the limit of safety to leave on a tourniquet. An anaesthetic is always indicated because of the pain and because the patient will resist muscle pull and lastly because one has to do things in a compound fracture that one's patient could not stand if he were not anaesthetized. The surrounding area is shaved, cleaned with gasoline, ether and iodine. The wound is wiped out with alcohol. It is necessary to know if the wound has been caused from without or from within. If from without one would expect more laceration and it would cause one more concern as the danger from infection is greater. If

a piece of attached bone is protruding it must be cleaned off with alcohol and put back in place for three reasons, because it may live, it stimulates new bone formation and if one leaves it, one has a bridge around which new bone will form. Then vessels, tendons and nerves are located and repaired. Any loose particles of bone or any foreign bodies are removed. Approximation of the ends of the bones, proper alignment and immobilization are then carried out with the limb in the best position to accomplish this. The wound is then stitched up and if it was caused from within out, an alcohol dressing is put on and immobilization is carried out in plaster or extension as required. If however the wound is from without in, leave one end of the wound open for drainage and have a window put in the plaster to change the dressing. If the fracture is of the femur and is a bad one, it is advisable to leave it at rest for twenty-four hours applying cold compresses only, because of the danger of a Volkmann's paralysis developing. This also applies to a supra-condylar fracture of the humerus and occasionally to a fracture of the forearm. If gas gangrene is going to set in, it will be there within twenty-four hours. The wound is painful, may crackle, has a brick-coloured tinge and there is a bloody thin discharge. The odour is typical and pressure will cause gas bubbles. Later microscopic examination will reveal the bacillus *Welchii*. The child will be very ill and may be so toxic that he says he feels fine. The treatment is prompt amputation if one feels that the child has a chance.

A supra-condylar fracture of the humerus is the most common fracture of the extremities met with in children and occasionally occurs as the result of a motor accident. The reason for this is that the child when struck falls on his out-stretched hand and the bone at the point of fracture, above the epiphyseal line, is new-growing and breaks more easily. The diagnosis of a fracture must be distinguished from a dislocation which may give one the same picture i.e. a hollowing out above the elbow,

radial displacement and a change in the carrying angle. The method of differentiation is that in a fracture one may get crepitus and the relationship of the bony parts remain undisturbed, whereas in a dislocation, the olecranon will be shoved back and will be above the plane of the two condyles. X-ray will confirm one's diagnosis. The manipulation for reduction is to pull the forearm forward, put up in extreme flexion, correct any radical displacement and see that the thumb is out beyond the shoulder of the same side in forearm supination.

In children, fractures do not need to be immobilized quite as long as in adults, probably about two-thirds of the time required by an adult. According to X-ray evidence at one of the children's hospitals there are ten fractures to every slipped epiphysis.

Injury to Abdominal Organs.

Rupture of an organ in the abdominal cavity is occasionally met with as the result of a motor accident. One hospital reports three cases of ruptured kidney during the past summer. The symptoms consist of severe shock to the child with pallor and falling blood-pressure. This is followed by nausea, vomiting, pain in the loin shooting down to the thigh, localized tenderness and perhaps swelling over the injured organ and haematuria. In slight injuries the haematuria is of short duration, but in more extensive lesions it may be severe and so persistent as to threaten the life of the patient. The passage of clots down the ureter may give rise to renal colic and obstruction may lead to total suppression of urine on that side. In some cases the bladder may become greatly distended with clots, the blood coagulating after entering the viscus. Haemorrhage into the perinephritic tissues is indicated by the formation of a swelling in the loin. Laceration of the peritoneum is followed by distention of the abdomen, increased anaemia from persisting haemorrhage and the onset of peritonitis. The development of a perinephritic abscess is recognized by fever, rigors, in-

creased pain in the loin and the usual phenomenon of deep suppuration.

The treatment is to put the child to bed and keep quiet and warm. Put an ice-bag to the loin and strap the affected side to relieve pain. If the condition is no worse by the fourth day, healing will likely take place. About 85 per cent. of these cases get better without surgical interference.

For persistent haemorrhage the hypodermic administration of ergot may be tried. If the haemorrhage is very severe a laparotomy is done. A slight laceration may be satisfactorily treated by sewing up with a mattress suture stitch. A severe laceration would indicate removal of the organ. If the blood doesn't escape externally, then one gets rapid swelling of the loin, increased anaemia, increased pulse rate and operation would be indicated. Clots in the bladder should be washed out through a large-eyed catheter.

Injury to the spleen will give rise to shock, as evidenced by increased pallor, coldness of the patient, rapid pulse, low blood-pressure and shallow rapid respiration. There will be pain in the left hypochondrium and the blood will collect in the left groin, going down towards the pelvis and not to the right side, due to the attachment of the mesentery. If severe it may be confused with a ruptured superior mesenteric vessel, but the local signs may decide this and on laparotomy, if the latter, there will be blood in both flanks. Severe sudden haemorrhage from the spleen may be controlled by pinching the vessels at the hilus. Splenectomy is the rule in such cases unless the internal haemorrhage is so severe as to prove fatal before a laparotomy can be carried out.

The liver may also be injured due to crushing, and the symptoms are those of shock, pain and local tenderness over the injured area and evidence of internal haemorrhage. If the latter continues a laparotomy may be done and an attempt made to arrest the haemorrhage, but this is difficult.

As a remote possibility the urinary bladder may be ruptured by a motor accident, especially if it is full. The treatment is immediate laparotomy and stitching up the bladder.

A point in the gastrointestinal tract may rupture as the result of an accident. The duodenum seems to be the most frequent site. The child suffers from severe and usually lasting shock, accompanied by intense abdominal pain. If there is marked tympany, it means perhaps that there is free air in the abdominal cavity from the open intestinal canal and one gets absence of liver dullness on light percussion. If one hasn't the latter, however, one can't be sure whether free air is present or not. Even if the injury is low down one practically always gets vomiting. The abdominal contents may escape from the bowel especially if it is a small bowel injury, and may be mistaken for blood. There may be one bowel movement and likely a little blood with it. If rupture is fairly certain laparotomy should be carried out at once before the onset of acute peritonitis.

Chest Injuries.

Chest injuries are rare in children as the result of motor accidents. Diagnosis is made from the history, signs of local trauma, pain, dyspnoea, and restricted chest movements. Contusion may occur without fractured ribs in a child. The symptoms are severe pain in the chest, with perhaps temporary shock and slight haemoptysis. An inflammatory reaction of both lung and pleura follows and the treatment is to keep the child quiet and warm and strap the affected chest and regulate normal function. Severe laceration of the lung will cause marked shock, pain and dyspnoea. Evidence of haemorrhage soon follows as haemoptysis or haemothorax or both. If the bleeding is severe the patient may die from asphyxia, due to the blood filling up the larger bronchi. Haemothorax is evidenced by an increasing dullness with loss of breath sounds

coming on soon after the injury. This rarely requires special treatment since the blood soon clots and is readily absorbed. But if it causes marked dyspnoea it should be aspirated. If from the laceration the air escapes rapidly into the pleural cavity, this will cause collapse of the lung and a pneumothorax. If much air has escaped as-

piration will be necessary to relieve dyspnoea. If, however, only a little air has escaped, then, when the lung begins to heal, this air is absorbed and the lung gradually expands. This takes about four or five days. Surgical emphysema may result from a wound of both lung and parietal pleura, but is not considered serious unless extensive.

*Bone Tumors.

By T. D. Kendrick, B.A., 2T8.

In this paper the attempt is made to give a concise description of each clinical entity occurring in the Classification of the Registry of Bone Sarcoma.

Each type is discussed under etiology, pathology, signs and symptoms, and X-ray findings, prognosis and treatment.

The immense amount of work accomplished by this committee, formed by some of the most outstanding pathologists and surgeons on the continent, in collecting and classifying all the available data on Bone Tumors, has provided a systematic basis for study and their classification replaces the former hopeless chaos of nomenclature.

According to the Registry, all tumors of bone fall into one of the eight types, as follows:

1. Metastatic tumors of bone.
2. Periosteal Fibrosarcoma.
3. Osteogenic Tumors.
 - (a) Benign.
 - (b) Malignant.
4. Inflammatory Conditions.
5. Benign Giant Cell Tumor.
6. Angioma.
 - (a) Benign.
 - (b) Malignant.
7. Ewing's Tumor.
8. Myeloma.

In the words of Bloodgood:

"It is essential to make a differential diagnosis because the vast number of bone lesions to-day are not malignant and unless you can make a differential diagnosis, you will mutilate for a benign tumor."

1. Metastatic Tumor of Bone.

This group is composed of *carcinoma* developing in bone from a primary site most frequently breast, prostate, hypernephroma or thyroid gland.

The tumor mass develops near the *centre* of a bone close to the entrance of the nutrient artery. Secondary to carcinoma of the breast the bone lesions are usually widespread resembling multiple myeloma in distribution. Prostate metastases usually locate in pelvis, lumbar spine, femur or sacrum; in this case the picture is one of increasing density with sclerosis and laying down of calcium. The secondaries of hypernephroma affect chiefly the bones of the upper part of the body and the striking bone change is osteolytic with rarefaction.

The tumor cell is usually true to the type cell of the original carcinoma.

Clinically, we have a history of the original tumor with operation for removal followed by a period with complete absence from symptoms; this period is important in making the diagnosis. Pain develops rather suddenly in a bone; it is very severe and continuous in character.

* A paper delivered before the Alpha Omega Alpha Honorary Medical Fraternity, November, 1927.

Roentgen ray reveals a lesion located centrally in the bone. It has a moth eaten appearance with ragged edges.

The prognosis in metastatic tumor is always unfavorable; the only exception is a solitary metastasis from carcinoma of the thyroid or from hypernephroma which may result favorably if removed along with the original focus.

Treatment consists in removal of the tumor and primary focus. The other method of treatment is radiation by radium or X-ray. Most favorable results have followed heavy doses of Roentgen ray on carcinoma in the lumbar spine secondary to prostate. Frequently relief from pain is very rapid and persists for several months. The partially destroyed vertebrae may exhibit fibrosis and even recalcification.

2. Periosteal Fibrosarcoma.

Very few cases are on record; distinction from fascial sarcoma is very difficult, often impossible. Periosteal fibrosarcoma may occur at any age.

This tumor arises from the outer fibrous layers of the periosteum; however, despite its intimate relation to periosteum, it leaves the cortex of the bone intact. The point of origin of the neoplasm is frequently at the insertion of tendons or dense fascia. The mass remains encapsulated for a long time and pushes aside rather than destroys the soft tissues.

On gross section it presents a firm, fibrous, white, glistening appearance. Microscopically it is made up of fusiform fibroblasts which are incapable of producing bone.

The symptoms are those of osteogenic sarcoma viz.: pain, swelling and impairment of function with this exception that pain usually occurs rather late. By palpation, the periosteal attachment cannot be detected and even at operation the presence of periosteum is frequently missed; although this periosteal attachment is usually broad the tumor is often freely moveable.

X-ray shows a faint shadow with indistinct outline through which runs the

grossly intact shaft of bone. There is no deformity of the bone.

Radical surgical removal often results in a permanent recovery. Less careful curettment may be followed by recurrence with a tendency to form metastases and a gradual acquisition of malignant characters. The removal of the tumor mass should therefore be followed by a prophylactic dose of X-rays.

3. Osteogenic Sarcoma.

(a) *Benign.*

This comprises the well-known group Exostosis, Osteoma, Chondroma, and Fibroma. All have essentially the same structure, the only variable being the type of connective tissue cells predominating. Description of these tumors is exhaustive in text-books.

Exostoses occur usually in persons between the ages of ten and forty years in the ends of the long bones particularly the lower end of femur and upper end of tibia or humerus.

The tumors appear to be more or less completely made up of bone although varying amounts of cartilage or fibrous tissue may be present. The outer end of the growth projecting into soft tissues is covered by a bursa.

The patient notices a painless swelling or deformity. X-ray shows a cortical point of origin in the diaphysis near the epiphyseal line; it penetrates rather than invades the soft tissues.

Treatment consists in thorough excision of bursa, capsule, cartilage and bone; this may be followed by cautery or X-ray. Recurrence is said to occur in ten per cent. of cases.

Osteomas. "Osteomas present similar clinical characteristics but are composed of compact bone. There is no metastasis."

"*Chondromas* occur in the medulla, are usually of slow growth and are practically always local." Their site is most frequently in the cancellous bone close to the epiphyseal line.

Symptoms do not appear early; there may be a slight pain and the bony cortex may bulge slightly.

The X-ray shows a cystic tumor with irregular trabeculations of bony or calcareous deposits *and shows invasion of the epiphysis*. The periosteum is expanded but rarely involved and there are rarely metastases. Marked deformity is not infrequent and fracture may occur.

Chondromas react very readily to radiation therapy, the tumor rapidly shrinking in size and being transformed into a solid bony mass.

True *Fibromas* are very rare.

(b) *Malignant Osteogenic Sarcoma.*

The term osteogenic tissue means tissue which if developing normally would eventually form bone, not that it always does form bone. Malignant bone tumors occur at the rate of about one per 100,000 population on this continent.

In the formation of a malignant osteogenic sarcoma, two forces are at work: the growing, expanding force of the tumor and the body reaction manifested by rapid proliferation of the cells of the periosteum. The tumor encounters little resistance in filling the whole medullary cavity; it then permeates the cortex by way of the Haversian system and encounters the bony shell formed by the hyperactive periosteum. By the time this shell has been perforated another has been laid down. Thus a race is established between the expansive power of the tumor and the vigorous attempts of the periosteum to keep it hemmed in. Very soon however the tumor growth overcomes the defense and the periosteum itself is perforated. The neoplasm then spreads rapidly through the soft tissues and shortly is pressing on the skin; *this is never invaded by osteogenic sarcoma*.

Malignant osteogenic sarcoma is a disease of adolescence, occurring most frequently between the *ages of ten and twenty years*. This age corresponds with the period of most energetic skeletal development and suggests a possible factor in etiology.

The point of attack is the *metaphysis of long bones* most frequently the femur, tibia and humerus; eleven cases

are found in the lower limb to one affecting the upper extremity.

The gross structure consists of rods of hyaline osseous tissue arranged like spikes of a wheel *perpendicular to the long axis of the involved bone*, or like fluffy trabeculae spread beneath the periosteum on top of the cortex of the involved portion of the bone. In the X-ray, the first structure is represented by the classical sun-ray like appearance.

Histologically an osteogenic sarcoma is a mass of fibrous tissue showing spindle cells; if round cells predominate, the tumor is not an osteogenic sarcoma.

Pain, swelling and impairment of function is the triad of symptoms in bone tumors. The *pain* of osteogenic sarcoma appears early and is excruciating and continuous. It keeps the patient miserable by robbing him of his sleep. The pain is caused by pressure of the tumor mass on the highly sensitive periosteum and may sometimes be relieved by drawing up the leg so as to relax the muscles overlying the tense periosteum.

The outlines and consistency of the *swelling* can be defined by careful palpation. Frequent palpation is one of the best guides to the progress of the disease.

The X-ray picture shows lack of definite, limiting outline to the tumor and shows lifting of the periosteum at the extremities of the growth where the periosteal cells are able to heap up and form bony material. Often the old cortex appears grossly intact, running through the centre of the tumor mass.

Malignant osteogenic sarcoma is invariably fatal due to general exhaustion of the patient and to lung metastases; *the average duration of life from the onset of the disease is only twenty months*.

Treatment: Two old methods, viz.: Coley's fluid and Ligation of the main artery supplying the tumor never cured a case of this type of sarcoma and have now been discarded in favor of Radical Surgery or Radiation.

"The theory underlying the former is that by early diagnosis combined with radical surgical treatment usually mean-

ing amputation with disarticulation, the problem of therapy in bone sarcoma may be solved as it occasionally is in some types of early diagnosed and well localized carcinomatous lesions.

There are some obvious contraindications to radical surgery:

1. If removal and eradication of the primary tumor is impossible. This immediately rules out the spine, skull and pelvis.

2. There must be absence of clinical evidence of metastatic generalization of the tumor; this of course includes Roentgen ray films of lungs and whole skeleton.

In case Radical Surgery is decided upon it has been proven that lung metastases appear just as soon following disarticulation as following amputation distal to the hip joint.

Radiation, the most recent method of treatment will probably yield much better results when it is used with the same skill as the scalpel. The effect of radiation on living tissue whether stimulation or inhibition, depends on the dosage. Inefficient radiation may stimulate the tumor.

4. Inflammatory Conditions of Bone.

The three most commonly occurring conditions of inflammatory origin producing swellings of bone and often confused with newgrowths are: Myositis Ossificans, Osteomyelitis and Osteitis Fibrosa Cystica.

The first, *Myositis Ossificans* is a change taking place in various muscles especially those of the back by means of which bony material replaces the fibrous interstitial tissue, thus transforming the muscles into bony plates or rods.

Osteomyelitis is classified as traumatic e.g. ossifying hematoma, syphilitic, infectious, e.g., Brodie's abscess. Differentiation of osteomyelitis from certain types of bone neoplasm is one of our most difficult problems. It sometimes requires analysis of clinical findings, Roentgen ray and even biopsy before the diagnosis is complete.

The third condition—*Osteitis Fibrosa*

Cystica is on the border-line between inflammatory reaction and new growth.

It occurs most commonly under the age of twenty years as a fibrocystic degenerative change in the diaphysis of long bone—most commonly the shaft of the humerus or the upper end of the femur. Healed cysts can often be demonstrated by X-ray at the site of old healed sprains or fractures. This cystic disease may occur in generalized form and is then familiarly known as Von Recklinghausen's disease. The lesions are of slow growth with little or no pain and seldom recognized till X-ray has been taken or fracture has occurred. In later stages careful palpation may reveal a smooth painless thickening of bone without local signs of inflammation. Joint movement is not impaired.

The Roentgen ray picture discloses a mass of fibrous tissue in itself indistinguishable from sarcoma but completely surrounded by a definite shell. The bone destruction is all within this shell and there is no evidence by X-ray or palpation of tumor outside.

Prognosis: Metastases are unknown; *central tumors of bone which are not metastases or multiple myeloma are seldom malignant*. The treatment consists in curetting out the tumor mass and allowing the cavity to granulate in or better, fill the space with a bone graft.

5. Benign Giant Cell Tumor.

The patient is usually *between the ages sixteen and twenty-five years*, considerably higher than in osteogenic sarcoma. The site is in the *epiphysis* of a long bone, most frequently the bones meeting at the knee or in the distal epiphysis of the radius.

The gross specimen is spherical in shape and enclosed in an osteomembranous capsule; it is red in color and jelly-like in consistency resembling exuberant granulation tissue and containing no vestige of original bone.

Microscopically it consists of giant cells embedded in fibroblastic tissue. The giant cells are of foreign body type containing from ten to sixty centrally-placed nuclei. The giant cells are massed just under the periosteum and con-

stantly destroy the cortex from within while the periosteum lays down an advancing shell of new bone, thus preventing the tumor mass from early perforation and involvement of adjoining structures. The epiphyseal cartilage is very resistant so that the *diaphyses and joint cavity are rarely involved*. Nothing contributes more to hastening of a perforation than an exploratory incision.

Giant cell tumors occur characteristically in the epiphyses of young adults with pain and swelling as initial symptoms. The disease progresses slowly and in from three to eighteen months, *disturbance of function* becomes the chief complaint. Injury apparently plays a stimulating role in the growth of this tumor.

The X-ray shows a diffusely mottled, rarefied area produced by the bone absorption activity of the ever-expanding growth; the tumor mass is surrounded by a thin usually intact bone shell. It is vividly described as a "soap-bubble" appearance.

Giant cell tumor is practically always benign; metastases do not occur.

This neoplasm is treated either by Radiation or Curetting. Radiation causes the tumor to increase in size for two or three months; malignant changes may be suggested; the bone shell expands and then becomes thin and melts away. The overlying skin becomes inflamed. But following this destructive stage, a productive stage ensues with constant shrinkage of the tumor and formation of new dense bone.

The second method of treatment is curettment followed by chemical and thermal cautery. Bloodgood claims no recurrence after this method in two hundred and fifty cases; Kolodny reports recurrence in twenty per cent. of his cases; thorough curettment should be repeated as often as the tumor recurs.

6. Angioma.

(a) Benign.

"Benign angiomas occur in bone as cavernous structures similar to cavernous angiomas in the soft parts. Roentge-

nologically they rarefy bone and expand it, in something the same way that giant cell tumors do, but having more and smaller loculi." They are found most frequently affecting the cranial bones or the upper end of the tibia. Treatment consists in curetting followed by chemical cautery. They do not recur or produce metastases.

(b) Malignant.

Malignant angiomas of bone are rare; many supposed angiosarcomas are probably telangiectatic osteogenic sarcomas. These tumors are very vascular; they resemble adenoma in the presence of alveoli and tubules; they are made up of large polyhedral cells with well-defined, pale, vesicular nuclei.

The Roentgenogram shows the results of two forces at work: the destructive—with complete washing out of the bone shadow and the productive with formation of large bulky bone growths.

Clinically these neoplasms closely resemble osteogenic sarcoma and the differential diagnosis can only be made on close study of the historical structure. Angiomas occur in old or young. Pain occurs later than in osteogenic sarcoma; these tumors may attain a very large size.

The disease is invariably fatal, often in a few months. Metastases are early; some believe the tumor to have multiple origin. No surgical cures are on record and no improvement follows radiation.

7. Ewing's Tumor.

This lesion is three times as frequent in males as females and is most frequent between the *ages of five and fifteen years*. The commonest bone to be affected is the tibia, followed in order by the fibula, humerus, ulna and femur; often in the small bones of the extremities. It is the *shaft* and not the epiphyseal ends which are usually affected. Simultaneous tumors in several bones are common.

Ewing's tumor often begins simultaneously in numerous areas of the involved portion of bone, in the bone marrow filling, the medul-

lary cavity, as well as the large Haversian canals; it rapidly enlarges, becomes confluent and expands in all directions. The bone lamellae are shoved apart giving the characteristic *longitudinal striation in X-ray*. The tumor breaks its way through the periosteal shells as in the case of malignant osteogenic sarcoma.

The tumor is made up of small polyhedral cells with round or oval nucleus and scant, clear, stainless cytoplasm. There is a *complete absence of intercellular material*; diffuse bone absorption is characteristic.

When in a young person a seemingly trivial trauma is followed by an insidious onset of fever and intermittent limping due to recurrent aching bone and is accompanied by a slight or no increase in leucocytes, a tumor is more probable than is osteomyelitis."

Slight trauma is an almost constant factor in the history of Ewing's tumor. The pain resembles that of Malignant Osteogenic Sarcoma but is *intermittent* in character; for several weeks at a time it may be entirely absent. Fever and a leucocytosis of twelve to fifteen thousand accompany the attacks and between attacks the swelling is persistent; the skin is never involved; joint invasion is unknown.

Roentgen ray shows a diffuse involvement of half the length of the bone with no shaft left. There is no lifting of the periosteum at the extremities of the tumor. The rapid response of Ewing's tumor to radiation is a therapeutic test which should replace incision.

This neoplasm is invariably fatal; the *average duration of life from the onset of the disease is three years* as compared with twenty months for malignant osteogenic sarcoma. The prognosis does not vary with the age of the patient. Metastases locate in skull, lung or other bones; they are accompanied by severe febrile reaction and the patient, already greatly emaciated, soon dies.

Treatment consists in application of radium after immobilization of the limb to prevent fracture. The tumor rapidly diminishes in size but tends to recur

and become resistant to radiation. When it recurs locally, excise or amputate. Pulmonary metastases may disappear for years following radiation.

8. Myeloma.

Only 9 cases are reported in the Registry. Myeloma occurs in *males forty to sixty years of age*. It effects the midportions of long bones especially the humerus, femur and flat bones.

The nodules of the growth vary in size from a bean to an orange. The gross picture is that of a thinned cortex with increased medullary substance; there are no bony trabeculae; bone destruction is more rapid but less diffuse than in Ewing's tumor. The cortex is eroded and periosteum is pushed away. The periosteum repeatedly forms new layers which are rapidly perforated by the oncoming tumor. Bending and fracture are frequent.

Histologically the tumor cells closely resemble plasma cells and there is little or no intercellular substance.

Patients suffering from Myeloma usually give a history of trauma. Pain is an important symptom, but occurs later in this disease than in malignant osteogenic sarcoma. At the commencement there is a slight fever which is soon followed by a subnormal temperature.

Palpation reveals crepitation of the thinned cortex; the regional lymph glands and the spleen are enlarged.

Metastases in other parts of the skeleton are present almost from the first; in fact some authors believe the lesions to arise simultaneously. Emaciation and intoxication are extreme, due to extensive bone marrow destruction. Metastases in lungs are rather infrequent at least till a late stage.

Roentgen ray discloses the situation and multiplicity of the lesions. The picture shows a well-outlined, definitely circumscribed area of diminished density. The cortex is thin and wavy in outline although perforation of the cortex is rare. X-ray pictures of the entire skeleton should be obtained. Exploratory incision is very undesirable and unnecessary since the prompt reaction of

the tumor to radiation furnishes a good therapeutic test of its identity.

Myeloma is always fatal; occasionally the prognosis is more favourable than in other malignant bone tumors; cases are recorded of patients living ten years after the onset of the disease.

Treatment consists in immobilizing the limb to prevent fracture and exposure to heavy doses of X-ray; these should not be continued when the leucocyte count reaches as low as two thousand five hundred.

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Case Report of Pyelitis in a Child.

By L. N. Silverthorn, M.B.

A typical case of Pyelitis is here reported. The past history suggests the probability of the present illness being an acute exacerbation of a chronic condition. In this case a definite course of treatment was followed.

Case History.

The patient was a girl, B.M., four years of age, admitted to the children's ward of the Amasa Wood Hospital, St. Thomas, Ontario, July 6th, 1927.

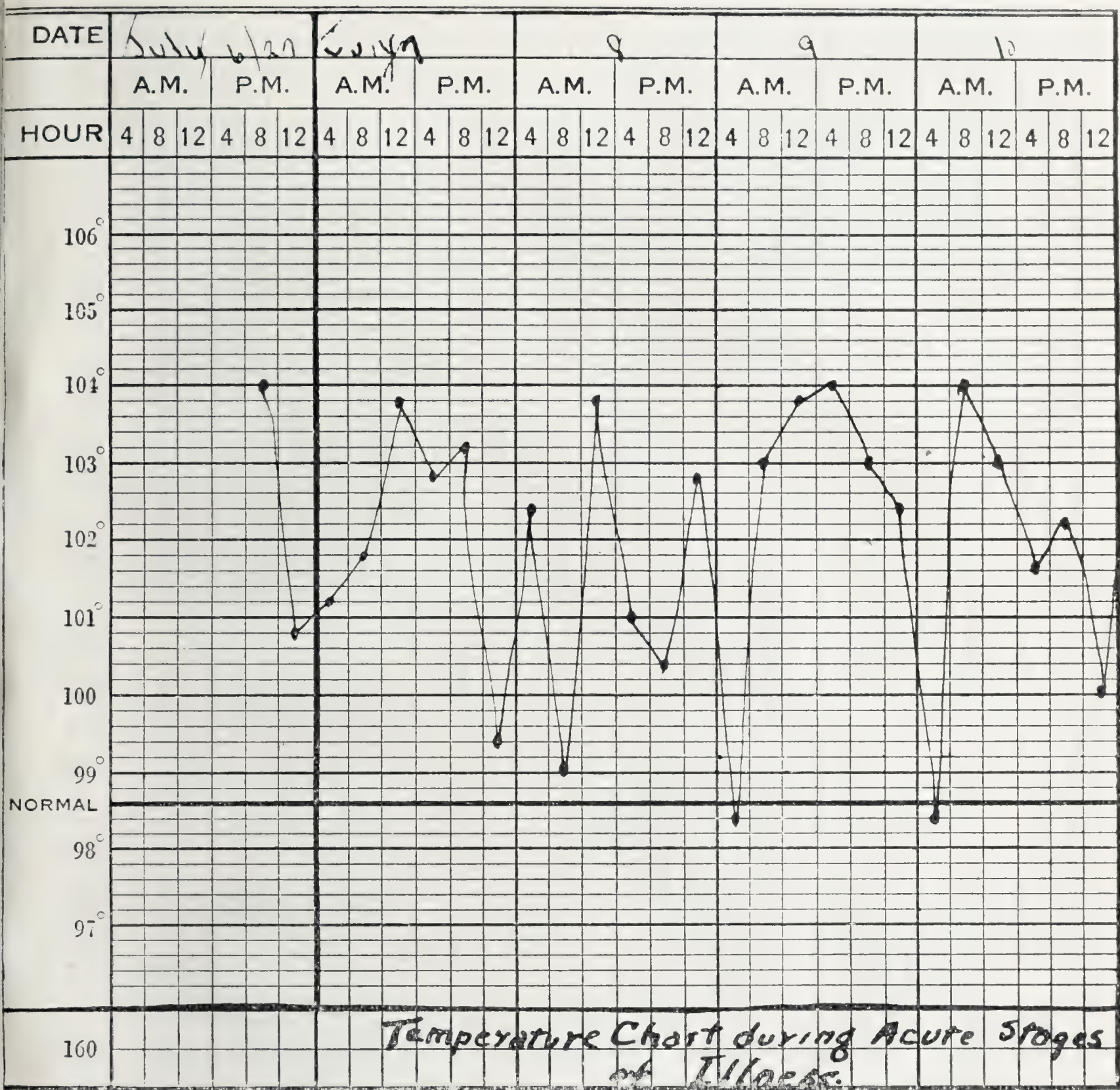
Complaint. The mother stated that the child had been feverish, fretful and drowsy. She had had a poor appetite and complained of "stomach-ache." All these symptoms had been present for ten days.

History. The child had been perfectly well until ten days before admission. She then became feverish and fretful. The feverishness continued for two days. The condition then improved until three days before admission, when the fever recurred. At the same time the patient complained of some indefinite abdominal pain which was present until admission. In addition to other symptoms she complained of headache. The family history has no bearing

on the case. The only point of interest in her past history is the fact that she had had pains in the stomach and attacks of fever with frequency of urination one year ago and occasionally during the Winter of 1927.

Physical Examination. The child appeared acutely ill. She was well nourished and developed, and on admission had a temperature of 104°F. The skin was dry, hot and slightly dehydrated, but no rash was present. The examination of the throat and ears showed some evidence of infection. The Respiratory and Cardiovascular systems were not remarkable. On the examination of the abdomen there was some tenderness on the right side from the costal margin to the pelvis. The muscles of this side were somewhat more rigid than on the opposite side. Rectal examination revealed nothing of interest. No other abnormal findings were noted.

Laboratory Report. A catheter specimen of urine was obtained which showed an opalescent acid urine. Acetone was present, as demonstrated by Rothera's test. Microscopic examination revealed the presence of 16-20 pus cells per high power field. After treatment

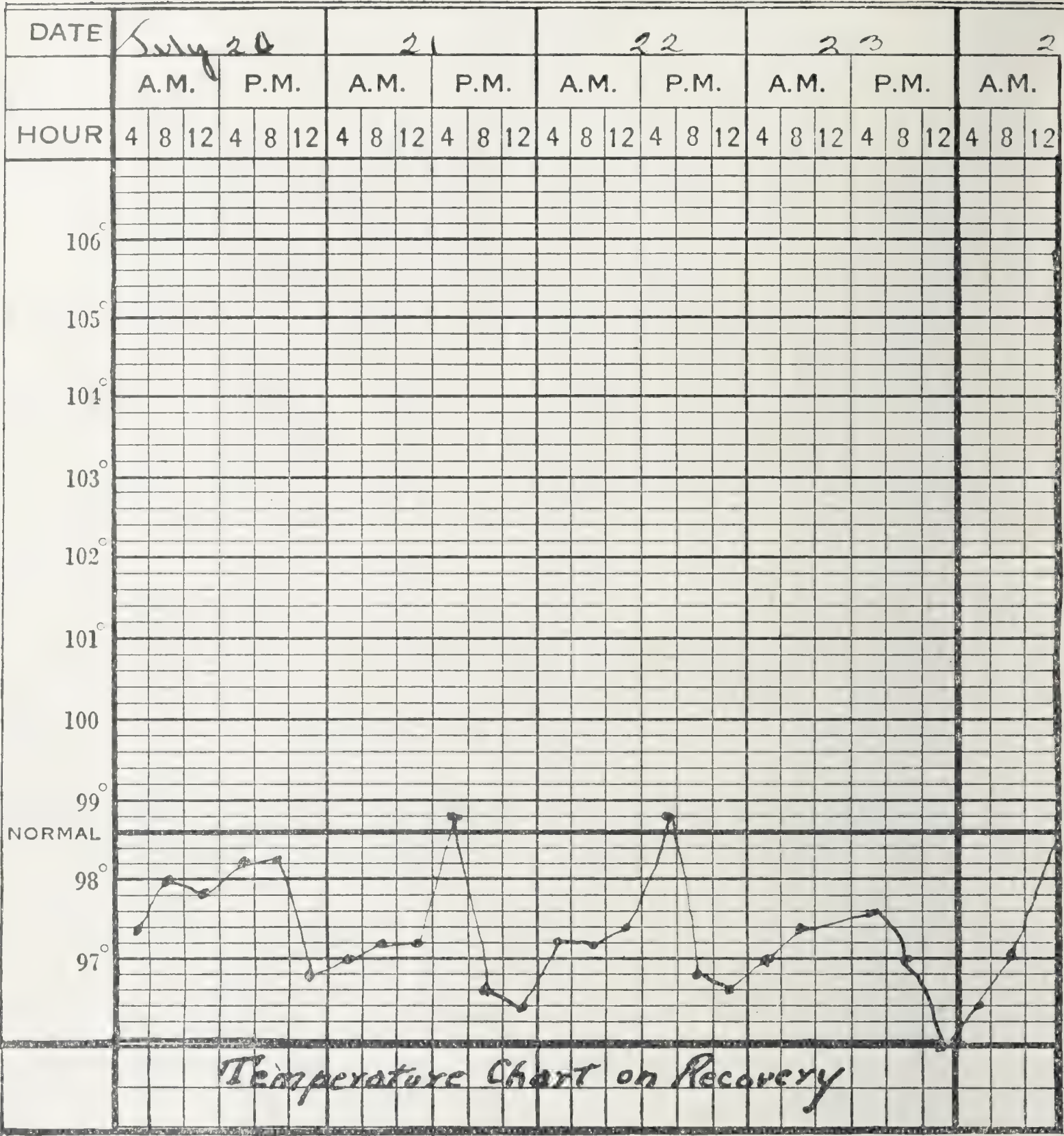


was started the urine became alkaline. From July 8th until the 17th the pus cells varied daily between 8 and 70 per high power field. - From July 17th until discharge, eight days later, the number of pus cells in the urine decreased until only an occasional one could be seen. Every specimen of urine was tested for alkalinity. A catheter specimen of urine was cultured and showed the presence of Colon Bacilli.

The Blood Count on admission was: Red Cells, 5,120,000 per cubic mm.; White Cells, 15,800 per cubic mm; Polymorphonuclear leucocytes, 72 %

and Lymphocytes 28%. Haemoglobin 90%.

Progress. The child was in the hospital from July 6th until July 24th, 1927 (18 days). The day after admission the urine was clear of acetone, but she seemed to be still slightly drowsy. Abdominal tenderness remained throughout her stay in the hospital, but was less marked during the last two days. For twelve days the child had a fluctuating temperature which suggested an active condition in the kidney. In this case, a very striking feature was observed, namely, that on days the tem-



perature was high, few pus cells were found in the urine. After a diuresis was established, pus cells were found in clumps in the normal level and an improvement in the clinical condition of the child was noted. From July 6th, 1927, to the 18th, her condition remained about the same. She then showed a remarkable improvement. The temperature dropped to normal until discharge. Only a few pus cells (3-4 per high power field) were found in the urine.

Treatment in Brief: (1) The child was put on an alkaline mixture of Potassium Citrate and Sodium Bicarbonate,

fifteen grains of each every four hours. (2) All food was discontinued and she was allowed only 15% Sugar Solution (2 oz.) every hour by mouth for twelve days. When her toxic appearance and clinical condition improved she was given the juice of two oranges, whole milk and water. Later her diet was increased, until she was discharged on a diet of alkaline-forming foods consisting in the main of vegetables, fruits (except prunes, plums and cranberries), milk, cereals and cheese.

Comment. The conditions one would naturally consider in this case are Acute

Nasopharyngitis, an Acute Abdominal Lesion and Pyelitis. The first of these conditions was not definite nor severe enough to be the only cause for the child's state. The fact that the child had been sick ten days, along with negative rectal findings, would make an acute abdomen an unlikely entity. In this case we find a Typical History of Pyelitis with sudden onset, irregular fever, pain and tenderness in the abdomen with pus in the urine.

The parents were instructed to follow a definite treatment with the child for at least one year after she left the hospital. This was done because Pyelitis is notorious for its recurrence. The mother was willing to co-operate and the child was given an alkaline mixture and a diet of alkaline-forming foods for the period of one year. So far, the patient is in good health and her mother states that she is still on the diet and her urine is alkaline. One of the big factors in

the recovery of this child is that a definite diuresis was obtained, the kidney pelvis being well flushed out. This medical drainage, I believe, is one of the essential points in the treatment.

Summary. A case of Pyelitis in a four-year female child is reported suggesting from the history an acute exacerbation of previous attacks of the same condition. The clinical course, Temperature Charts and Laboratory findings demonstrate a typical case. The child was given alkalis and 15% Sugar Solution by mouth, later adding a diet of alkaline-forming foods. The patient was discharged in good condition and has been perfectly well since.

References. (1) List of base-forming foods was obtained from "Common Procedures in the Practice of Paediatrics, Brown and Tisdall.

(2) 15% Sugar Solution formula from the Hospital for Sick Children.

Fall Sport Review—1927.

Rugby.

In the Mulock Cup Series the Senior Med. team was grouped with Senior School and Dents. Both these latter teams were very strong, especially Dents. The Med. team, despite the usual handicap of lack of time to practise, put up a good fight for the group title. They defeated Senior School in the first game, 8 to 1, but lost the next two games to Dents with scores of 11 to 1 and 10 to 5 respectively. Meanwhile Dents had defeated Senior School also and thus clinched the title. The kicking and running of Gordie Large and the plunging of Lawson featured the games. With a few men from the Juniors next year's team should be hard to stop before the finals.

The Juniors were placed with Junior School and Junior Arts. Junior Meds. had a fairly strong team this year and were ably helped by "Fat" Long of last year's Varsity team. They defeated Junior Arts 19 to 14 and 10 to 0,

but were unable to take the measure of the School men, and lost both their games against them. Hence the latter were able to take the group title, beating the Arts men twice. The Juniors showed an aggressive type of play and with a little more work will give a good account of themselves next fall.

Track Meet.

The Interfaculty track meet was held this year under adverse circumstances. It was postponed twice and was finally held in the rain. Medical athletics missed the help of the versatile Evan Shute and Les Black. However, they managed to stand third in the final results with 22 points, a few points behind their rivals, U.C. Mo. Mitchell ran a wonderful race in the half mile to tie for first place. Hugh Crawford was also a point winner for Meds in the pole vault. These men along with other Medical stalwarts, managed to keep Meds in the running.

Faculty Notes.

Mr. W. W. D. Williams, Secretary-Treasurer of the Medical Society, was our representative at the McGill Medical At-Home on December 16, 1927.

The Medical Players Club, a newly-formed organization operating without the official endorsement of the Medical Society, yet composed largely of undergraduates in Medicine, staged their first performance in Hart House Theatre in the week of December 13, 1927, presenting Masefield's "Locked Chest" and Moliere's "The Doctor in Spite of Himself," under the able direction of Mr. H. E. Hitchman. Although the enterprise was not a financial success, much favorable comment was received by the Club, and it is hoped that the undertaking will be repeated next year to better advantage.

Members of the Medical Society who attended the open meeting on December 7, 1927, heard a very stimulating and interesting address by Dr. T. C. Routley, General Secretary-Treasurer of the Canadian Medical Association and one time president of the Medical Society, University of Toronto. Dr. Routley's address is reproduced in part elsewhere in this issue. Dean Primrose, Hon. President of the Society, presided at the meeting and spoke briefly. An interesting item on the program was the presentation of the Shield won by the Fa-

culty as the second award for floats in the Centenary Parade. Mr. W. A. Donohue, president of the Students' Administrative Council, thanked the Society for the part taken in the celebration. The next open meeting is to be held in Hart House Lecture room on January 18, 1928. It is to be hoped that undergraduates will realize that these meetings are planned for them, that an attempt is made to make them as profitable and interesting as possible and that the Society Executive would feel very gratified if they were better attended.

A very flourishing social event of the season in the Faculty was the Graduation Dance held at Casa Loma on January 6. Watson's Orchestra provided the music and Mrs. Primrose, Mrs. Oille and Mrs. Ryerson were the patronesses.

With D. M. Campbell as chairman of Daffydil we are assured of a top-notch performance this year. February 9 and 10 are the dates followed by the banquet on February 11. The banquet is to be thrown open to all undergraduates with the idea of making it a Faculty dinner.

The Medical At-Home is to be held at the King Edward Hotel on January 31. It is planned to accommodate all who wish to attend, and the committee will be greatly assisted if those wishing to go will sign the lists as soon as possible.

The Senior Medical At Home

KING EDWARD HOTEL

In the Crystal Ballroom

January 31st, 1928

Romanelli's Orchestra in Attendance

The Premier Medical Social Event of the Season

RESERVE THIS DATE

